

2. Non-Technical Abstract

Malignant melanoma is becoming increasingly common. While surgical excision is an effective treatment for patients with early and localized disease, the outcome for patients with metastatic disease remains quite poor. Recent advances with various forms of immunotherapy for patients with advanced melanoma have demonstrated a small, but significant, number of clinical responses with treatments involving the immune system. In addition, recent laboratory investigations have clarified the requirements for stimulating effective immune responses against melanoma. The use of normal skin to present a specific melanoma protein (antigen) may allow for effective stimulation of an immune response against tumor cells that also have this protein on their surface. The GP-100 gene will be used to modify skin cells to also express the GP-100 protein in an attempt to stimulate an immune response against melanoma cells which would also contain this GP-100 protein. In addition, use of the GM-CSF "hormone of the immune system" (cytokine) may better stimulate the normal cells containing GP-100 to better activate immune responses against the GP-100 protein. The new method of delivering genetic material (particle-mediated gene transfer) will be used to genetically modify the normal skin cells in this protocol.

This proposed Phase I trial will evaluate use of the "gene gun" to directly deliver genes for GP-100 and/or GM-CSF into human skin as a treatment strategy for patients with melanoma. Information about the side effects associated with this treatment will be determined. In addition, important information about two separate dose levels of genetic information will be obtained. Monitoring assays will determine the ability of the transferred genetic material to express the appropriate protein in normal human skin. In addition, laboratory assays will determine if immune responses against GP-100 can be simulated with this genetic vaccine approach. Finally, any anti-tumor activity resulting from this treatment will be measured.